UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/814,125	04/01/2004	Johan Frostegard	FROSTEGARD=1D	8029

1444 7590 06/12/2006

BROWDY AND NEIMARK, P.L.L.C.
624 NINTH STREET, NW
SUITE 300
WASHINGTON, DC 20001-5303

EXAMINER	
COOK, LISA V	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 06/12/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/814,125	FROSTEGARD, JOHAN	
	Examiner	Art Unit	
	Lisa V. Cook	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14 and 16-20* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-14 and 16-20* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/720,967.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Amendment Entry

1. Applicant's response to the Office Action mailed December 29, 2005 is acknowledged (paper filed 3/29/06). In the amendments filed therein claims 2, 9, and 17-20 were modified. Claim 15 has been canceled. Currently claims 1-14 and 16-20 are pending and under consideration.

2. Objections and/or rejections of record not reiterated below have been withdrawn.

NEW GROUNDS OF REJECTIONS

Please note: examiner was unable to ascertain if the instant claims were restricted from application number 09/720,967 now US Patent #6,780,605. Applicant is invited to shown evidence of such a restriction requirement.

Double Patenting

3. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

4. Claims 1-13 and 17-20 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-13 of US Patent #6,780,605 as evidenced by Muzya et al. (Immunologiya, 1997, Vol.6, pages 9-11, Abstract Only).

The instant invention and US Patent #6,780,605 are drawn to methods of evaluating cardiovascular disease from the measurement of the presence and/or concentration of antibodies to PAF which includes antibodies to phosphocholine. Muzya et al. are cited to show that antibodies binding to PAF by phosphocholine fragments. See abstract. Thus the inventions read on the same scope measuring the same disorder (cardiovascular disease) and detecting the same antibodies (aPAF). Accordingly, the instant method is encompassed by the claims in US Patent #6,780,605.

5. Claims 14 and 16 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-13 of US Patent #6,780,605 as evidenced by Muzya et al. (Immunologiya, 1997, Vol.6, pages 9-11, Abstract Only) and further in view of Baldo et al. (WO 87/05904).

Please see the discussion of US Patent #6,780,605 as evidenced by Muzya et al. and as set forth above.

Barquinero et al. as evidenced by Muzya et al. differ from the instant invention in not specifically teaching a means for testing comprising a ligand selected from the group consisting of phosphorylcholine and lysophosphatidylcholine.

However, Baldo et al. teach antigenic analogues of PAF (ligands) that are used to generate antibodies that bind PAF or antibodies to an antigen that binds aPAF. See claim 1 lines 6-7. The ligands including phosphorylcholine and is disclosed in the examples beginning at page 16 of the disclosure. Lysophosphatidylcholine structures are taught on page 30, for example.

The use of these ligands is taught to be useful because PAF is insufficiently antigenic to produce the necessary PAF-antibodies needed for immunoassay. The novel synthetic analogues (including phosphorylcholine) were sufficient to produce PAF-antibodies, which are suitable for immunoassay of PAF levels in biological fluids. See page 2 lines 4-12.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the ligand phosphorylcholine or lysophosphatidylcholine as taught by Baldo et al. in the measurements of antibodies to PAF and/or antibodies to an antigen(PAF) that binds aPAF as taught by Barquinero et al. as evidenced by Muzya et al. because Baldo et al. taught that PAF is insufficiently antigenic to produce the necessary PAF-antibodies needed for immunoassay. The novel synthetic analogues (including phosphorylcholine) were sufficient to produce PAF-antibodies, which are suitable for immunoassay of PAF levels in biological fluids. See page 2 lines 4-12.

One of ordinary skill in the art would have been motivated to employ the cited ligands in order to produce sufficient amounts of PAF-antibodies for immunoassay testing.

Response to Arguments

Applicants have submitted copies of Restriction Requirement responses to demonstrate that a restriction is of record in parent application number 09/720,967 now US Patent #6,780,605. However, this is not sufficient to ascertain the appropriateness of the obvious double patenting rejection set forth above.

Examiner needs to have a copy of the claims wherein the instant claims were previously presented in the parent application. Accordingly a ODP rejection has been presented.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

I. Claims 1-13 are rejected under 35 U.S.C.103(a) as being unpatentable over Barquinero et al. (Lupus, 1994, 3, 55-58) in view Muzya et al. (Immunologiya, 1997, Vol.6, pages 9-11, Abstract Only) and further in view of Ostermann et al. (Thrombosis Research, 52, 529-540, 1988).

Barquinero et al. teach an ELISA assay to measure antibodies against platelet-activating factor (PAF) in patients with autoimmune diseases. Specifically blood sample from patients with SLE (systemic lupus crythematosus), PAPS (antiphospholip syndrome), and syphilis. SLE is vascular diseases (relating to blood vessels). SLE includes severe inflammation of blood vessels (see The signet Mosby medical encyclopedia definition attached). See abstract and page 55 Introduction and page 56 "ELISA technique for anti-PAF".

With respect to the means for determining patients at risk for having cardiovascular disease and/or early atherosclerosis, it is noted that Barquinero et al. teach the measurement of PAF in patients with autoimmune disease such as SLE. SLE includes blood vessel inflammation, which could lead to cardiovascular disease (risk).

Barquinero et al. do not specifically teach the binding of PAF to antibodies of PAF comprising phosphocholine.

However, Muzya et al. teach that antibodies involving the ligand phosphatidylcholine (antiphosphatidylcholine antibodies) bind to PAF, lyso-PAF, and acyl analogs of PAF. The binding of antiphosphatidylcholine antibodies to PAF and its structural analogs is related to the presence of *phosphocholine* fragments. The binding of antiphosphatidylcholine antibodies to PAF was exemplified in the sera of women with obstetrical-gynecological disorders. See abstract.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use antibodies comprising phosphocholine as taught by Muzya et al. in the method and of Barquinero et al. because Muzya et al. disclosed that the binding of antibodies to PAF is related to *phosphocholine fragments* and the measurement of these binding complexes was useful in measuring obstetrical-gynecological disorders in women. See abstract.

Barquinero et al. in view of Muzya et al. differ from the instant invention in not specifically teaching PAF as an indicator for cardiovascular diseases such as atherosclerosis via PAF quantification in serum and plasma.

However, Ostermann et al. teach PAF quantification in serum and plasma as well as its correlation/diagnosis (discrimination) in Atherosclerotic patients. See abstract and page 531 2nd paragraph. Thirty-Six health volunteers and 40 atherosclerotic patients were evaluated in the study. Blood samples were analyzed to determine PAF concentration.

The results showed a significant increase in serum PAF levels of patients suffering from coronary artery disease. Page 536, last paragraph. The researchers also measured plasma levels. See page 538.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to measure PAF concentrations in serum and plasma patients with cardiovascular disease such as atherosclerosis as taught by Ostermann et al. in the method of Barquinero et al. in view of Muzya et al. because Osterman et al. teach the critical role of PAF in myocardial infarction/atherosclerosis and its accuracy of correctly classifying subjects. See abstract.

Ostermann et al. further teach that PAF could discriminate between low and high-risk groups and was an improvement over other commonly utilized discriminators (total cholesterol, VLDL/LDL-cholesterol, apo). See page 537 2nd paragraph.

One having ordinary skill in the art would have been motivated to do this because the early detection of such disorders is both beneficial in possible prevention and treatment of the disease.

II. Claims 14 and 16-20 are rejected under 35 U.S.C. 103(a) as being unpatentable over Barquinero et al. (Lupus, 1994, 3, 55-58) in view of Muzya et al. (Immunologiya, 1997, Vol.6, pages 9-11, Abstract Only) and further in view of Ostermann et al. (Thrombosis Research, 52, 529-540, 1988) as applied to claims 1-13 above, and further in view of Baldo et al. (WO 87/05904).

Please see Barquinero et al. in view of Muzya et al. and further in view of Ostermann et al. as set forth above.

Barquinero et al. in view of Muzya et al. and Ostermann et al. differ from the instant invention in not specifically teaching a means for testing comprising a ligand selected from the group consisting of phosphorylcholine and lysophosphatidylcholine.

However, Baldo et al. teach antigenic analogues of PAF (ligands) that are used to generate antibodies that bind PAF or antibodies to an antigen that binds aPAF. See claim 1 lines 6-7. The ligands including phosphorylcholine and is disclosed in the examples beginning at page 16 of the disclosure. Lysophosphatidylcholine structures are taught on page 30, for example.

The use of these ligands is taught to be useful because PAF is insufficiently antigenic to produce the necessary PAF-antibodies needed for immunoassay. The novel synthetic analogues (including phosphorylcholine) were sufficient to produce PAF-antibodies, which are suitable for immunoassay of PAF levels in biological fluids. See page 2 lines 4-12.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to use the ligand phosphorylcholine or lysophosphatidylcholine as taught by Baldo et al. in the measurements of antibodies to PAF and/or antibodies to an antigen(PAF) that binds aPAF as taught by Barquinero et al. because Baldo et al. taught that PAF is insufficiently antigenic to produce the necessary PAF-antibodies needed for immunoassay. The novel synthetic analogues (including phosphorylcholine) were sufficient to produce PAF-antibodies, which are suitable for immunoassay of PAF levels in biological fluids. See page 2 lines 4-12.

One of ordinary skill in the art would have been motivated to employ the cited ligands in order to produce sufficient amounts of PAF-antibodies for immunoassay testing.

Response to Arguments

7. Applicants contend that the combination of Barquinero et al. and Ostermann et al. did not disclose antibodies that bind phosphocholine. This argument was carefully considered and the reference of Muzya et al. (Immunologiya, 1997, Vol.6, pages 9-11, Abstract Only) has been added to address the limitation. Specifically, Muzya et al. disclosed that the binding of antibodies to PAF is related to *phosphocholine fragments* and the measurement of these binding complexes was useful in measuring obstetrical-gynecological disorders in women. See abstract.

Applicant's arguments against the reference of Karasawa et al. are MOOT because the reference has been removed. However, Karasawa et al. have been replaced with Baldo et al.

Applicant also contends that the objects in Barquinero and Ostermann and the present invention are different. Specifically, Barquinero and Ostermann do not use aPAF in risk assessment for developing vascular disease.

This argument was carefully considered but not found persuasive because Barquinero et al. are cited in combination with Ostermann. Ostermann teaches aPAF detection in atherosclerotic patients (atherosclerosis). The reference of Ostermann discloses disorders, which applicant argues are encompassed by the broad term cardiovascular disease. See page 9-10 of the response filed 3/29/06. While a deficiency in a reference may overcome a rejection under 35 USC 103, a reference is not overcome by pointing out that a reference lacks a teaching for which other references are relied. In re Lyons, 364 F.2d 1005, 150 USPQ 741, 746 (CCPA 1966).

Applicants argue that no motivation exists in Barquinero et al. to employ antibodies other than anti-PAF antibodies. This argument was carefully considered but not found persuasive because Barquinero et al. are cited in combination with Baldo et al. and Baldo et al. disclose the use of antibodies other than anti-PAF antibodies. Specifically Baldo et al. teach antigenic analogues of PAF (ligands) that are used to generate antibodies that bind PAF or antibodies to an antigen that binds aPAF. See claim 1 lines 6-7. One of ordinary skill would have been motivated to use these ligands because Baldo et al. taught that PAF is insufficiently antigenic to produce the necessary PAF-antibodies needed for immunoassay. The novel synthetic analogues (including phosphorylcholine) were sufficient to produce PAF-antibodies, which are suitable for immunoassay of PAF levels in biological fluids. See page 2 lines 4-12.

In response to the arguments that the use of phospocholine, phosphorylcholine and/or lysophophosphatidylcholine as a ligand provided for a more specific group of antibodies, it is noted that Baldo et al. teach the production of antibodies with these ligands. Accordingly, attorney's arguments of unexpected results cannot take the place of evidence in the record.

In response to applicant's argument that the examiner's conclusion of obviousness is based upon improper hindsight reasoning, it must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

8. For reasons aforementioned, no claims are allowed.

Remarks

9. Prior art made of record and not relied upon is considered pertinent to the applicant's disclosure:

A. Baldo et al. (LIPIDS, Vol26, No.12, 1991, 1136-1139) teach an immunoassay technique to measure PAF

10. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform to the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Group 1641 – Central Fax number is (571) 273-8300, which is able to receive transmissions 24 hours/day, 7 days/week. In the event Applicant would like to fax an unofficial communication, the Examiner should be contacted for the appropriate Right Fax number.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lisa V. Cook whose telephone number is (571) 272-0816. The examiner can normally be reached on Monday - Friday from 7:00 AM - 4:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, can be reached on (571) 272-0823.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group 1600 whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see httpr//pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Lisa V. Cook
Remsen 3C-59
571-272-0816
6/6/06

LONG V. LE 06/07/06
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600